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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte RONALD J. PETTIS, JAMES A. DOWN,
and NOEL G. HARVEY

Appeal 2010-006501
Application 09/606,909
Technology Center 3700
Oral Hearing Held: October 16, 2012

¹⁹ Before LINDA E. HORNER, STEVEN D.A. McCARTHY,
²⁰ and GAY ANN SPAHN. *Administrative Patent Judges*.

22 APPEARANCES:

24 ON BEHALF OF THE APPELLANT:

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38 The above-entitled matter came on for hearing on Tuesday, October
39 16, 2012, commencing at 1:05 p.m., at the United States Patent and

1 Trademark Office, 600 Dulany Street, Alexandria, Virginia, before Diane
2 Humke.

3 P R O C E E D I N G S

4 THE USHER: Calendar No. 30, Appeal No. 2010-6501, Ms. Coruzzi.

5 JUDGE HORNER: Thank you.

6 JUDGE HORNER: Okay. We've had an opportunity to review the
7 case and you've got 20 minutes, and you can proceed when you're ready.

8 MS. CORUZZI: Okay. Thank you very much. It's a privilege to be
9 in your room today. I'm here just to introduce my colleagues. Markus
10 Bergauer is an associate at Jones Day who has worked on this case with me,
11 and Robert West is a senior patent agent at Becton Dickinson, the assignee
12 of the patent application involved. I'll try to stay in my 20 minutes allotted
13 but beg your indulgence if we run over time.

14 This case is about the administration of insulin to a human subject into
15 the intradermal compartment, resulting in a systemic distribution in the
16 bloodstream superior to standard subcutaneous delivery. The sole issue on
17 appeal is obviousness. There were obviousness-type double patenting
18 rejections that are moot because those applications are now abandoned.

19 The examiner erroneously reached the conclusion of obviousness
20 based on three reversible errors: hindsight reconstruction, the examiner
21 unreasonably interpreted the claim term bioavailability and failed to consider
22 unexpected results in the record. If you should agree with me on any one of
23 those, you must reverse.

24 The claims at issue encompass administering insulin to a subject
25 through a hollow needle that penetrates the dermis of the subject's skin so

1 that the depth and exposed height of the outlet of the needle, which I'm
2 going to say is the orifice so that I don't have to keep saying depth and
3 exposed height of the outlet, is contained within a narrow target within the
4 dermis and then applying a pressure that's effective to control the rate of
5 delivery so that a specific what we call PK distribution of the drug is
6 achieved.

7 Two requirements of the pharmacokinetic, PK, profile are required by
8 the claim: a higher maximum plasma concentration, which is also called
9 C(max), and a higher bioavailability, which is defined as the area under the
10 curve, which I may refer to as AUC.

11 JUDGE HORNER: Okay. My understanding is one of the points of
12 contention here we need to decide is whether bioavailability is equivalent to
13 AUC or whether there are other means by which to determine
14 bioavailability.

15 MS. CORUZZI: Right. I mean, why don't we go to that point right
16 now. So, in this record, we've put in treatises, the Merck manual, that define
17 AUC as the most reliable measure of bioavailability. The Kasting
18 declaration, this is in the evidence appendix at E-194, he indicates that Claim
19 29, which recites the requirement of increased bioavailability, requires an
20 increased AUC, so he's equating AUC with bioavailability. And he, by the
21 way, is a Ph.D. from MIT. He's in the field at I think Procter & Gamble, a
22 reviewer of peer-reviewed journals. So he came to the conclusion that
23 Claim 29 requires a higher AUC.

1 JUDGE HORNER: And is the only place we find that is to sort of
2 infer it from the statement in paragraph 19, or does he come out somewhere
3 else in this declaration and state, you know --

4 MS. CORUZZI: No, it's in paragraph 19 when he states that the claim
5 requires an increased AUC. I'll find it for you in one second. Paragraph 19
6 on page 9, for example, Autret's pharmacokinetic profile does not exhibit
7 both an increased C(max) and an increased AUC, as required by the claims
8 of the Pettis application. So he's come to that conclusion.

9 There's another issue. In our reply brief at page 15, we address the
10 issue of the claims require both a C(max) increase and an increase in
11 bioavailability. The examiner contends that either one of those is a measure
12 of bioavailability. If that were the case, then our two limitations are
13 redundant and it's improper to read a claim to make one limitation
14 superfluous. And there are a number of recent Board of Appeals decisions
15 that have come down since our briefing. If I can read them into the record?

16 JUDGE HORNER: Yes.

17 MS. CORUZZI: Ex parte Mancie -- I have the Westlaw cites, I can
18 read that in -- 2012 Westlaw 407888; Ex parte Sexton, 2012 WL 334461;
19 and Ex parte Shukla, 2012 WL 1089015. And these all cite to a case called
20 Stumbo v. Ameristep, and that's a Federal Circuit decision, 508 F.3d 1358.
21 So since the claim requires two limitations to be elevated, if you took the
22 examiner's position, one of our limitations would be superfluous. That's
23 error, and we think it should be reversed.

1 JUDGE HORNER: What about the statement in the Merck excerpt
2 that says the most widely used general index of absorption rate is peak time,
3 so not C(max) but T(max) being an indicator of bioavailability?

4 MS. CORUZZI: But I believe the Merck manual goes on to say that
5 either T(max) -- here we go. However, peak time is often not a good
6 statistical measure because it's a discrete value that depends on frequency of
7 blood sampling, and in the case of relatively flat concentrations near the
8 peak, on assay reproducibility.

9 And with respect to C(max), the Merck manual says -- this is, I'm
10 sorry, E-122, page 2560 of the Merck manual, first column where it says
11 assessment of bioavailability. Bioavailability determinations based on peak
12 plasma concentration can be misleading because drug elimination begins as
13 soon as the drug enters the bloodstream. So the C(max) is the peak of when
14 absorption equals elimination, and the Merck manual says don't use that for
15 determining bioavailability. It's a measure you take to ultimately come to a
16 conclusion about bioavailability, but according to Merck, AUC is the most
17 reliable measure of bioavailability.

18 And we also relied on the Federal Circuit decision in Abbott v.
19 Sandoz, and this is in our brief at pages 17 to 18. And I'm not relying on it
20 for res judicata but for the fact that in a case at a similar time period
21 involving drug delivery, the Court, the District Court and the Federal Circuit
22 agreed that AUC is the measure for bioavailability, and that was uncontested
23 by the parties involved in the Abbott v. Sandoz case. So that's an external
24 data point if you will of evidence of how the skilled artisan would interpret
25 bioavailability and AUC. And again, that's in our brief at pages 17 to 18.

1 JUDGE MCCARTHY: But, counsel, I'm reading the passage from
2 the Merck manual here and it looks to me that they are conceding that the
3 most widely used general index of absorption rate is peak time, but then
4 they're giving their own opinion that AUC is better. Is there anything to
5 suggest in this passage that AUC is generally recognized as being a better
6 measure?

7 MS. CORUZZI: Well, I think the Merck manual is not just an
8 opinion, I think it's a treatise that the skilled workers look to, and I think the
9 Abbott v. Sandoz case is evidence of how workers in the field at the time
10 period, same time period as our filing date, viewed AUC as the measure of
11 bioavailability, as did Autret. I'm going to try my French. Biodisponibilité
12 was measured as AUC. Not C(max), not T(max), but AUC. And Autret is
13 one of the main references that the examiner's relying on. Did that answer
14 your question?

15 JUDGE MCCARTHY: Yes. Thank you.

16 MS. CORUZZI: Okay. Great. So using this nonconventional,
17 incorrect interpretation of bioavailability, then the examiner makes the
18 mistake of coming to the conclusion that Autret is the only reference that
19 reports a PK, none of the other references even report a PK or have a PK, the
20 vaccine art doesn't use PKs at all, vaccines are injected locally, cells eat up
21 the antigen and then travel into the lymphatic system. You don't have a PK
22 in the bloodstream, which is required by the claim. So Puri, D'Antonio and
23 Srivastava, you know, are just incorrect. It's an incorrect use of those
24 references. Autret is the only one, and in plain I would have said English,
25 but it's French, he basically says that there's no difference in bioavailability

1 (biodisponibilité), between subcutaneous and intradermal injections.

2 Mesotherapy was what it was called in the Autret reference.

3 So the examiner is taking the position that because Autret has an
4 increased C(max), and in his definition C(max) qualifies as equal to
5 bioavailability, that's his sole basis for saying Autret.

6 JUDGE HORNER: But doesn't Autret also have a lower T(max), so
7 it's got a faster absorption?

8 MS. CORUZZI: Well, T(max) is not -- hang on. Possibly. It's hard
9 for me to tell from the graph whether the ID occurred faster.

10 JUDGE HORNER: I think it was in the description.

11 MS. CORUZZI: He doesn't mention T(max) at all as far as I can tell
12 from the translation and the little bit of French that I can read, but he does
13 indicate that there's an increased C(max) but no difference in bioavailability.
14 And if you look at Table 1B3, you see the columns are ID, which is
15 intradermal, sub-Q, which is SC, BD, which is the French biodisponibilité,
16 which means bioavailability, and he finds no difference between sub-Q
17 injections and ID.

18 And again in the conclusion, in the discussion and conclusion on page
19 E4, Autret concludes in the discussion that these facts speak against a more
20 rapid or greater resorption put forward to justify mesotherapy, in other
21 words, ID, and that's in Column 1. And then the conclusion, it says in black
22 and white in French that there's a difference -- and this is calcitonin, not
23 insulin, but because we're talking about obviousness, we're considering it --
24 there's a difference in the C(max), but the biodisponibilité, bioavailability, is
25 not different after ID injection as opposed to sub-Q injection.

1 JUDGE HORNER: It seems like Autret is saying, and I'm looking at
2 page 4 of the translation under the section entitled Results, that T(max) is at
3 23.6, plus or minus 10 minutes with the subcutaneous route and 16.2, plus or
4 minus 7.5 minutes, with the ID route, and then later in more detail on page 6
5 they explain that for three of the subjects in the study, T(max) was earlier
6 with ID, whereas for three others it appeared at the same time, whatever the
7 route of administration. So it seems like at least in some of the subjects
8 T(max) was earlier, and then they say the average C(max) is significantly
9 higher with the ID route than with the subcutaneous route. So it seems like
10 if we were to take bioavailability, which we measure by T(max) or area
11 under the curve under the broadest reasonable interpretation, then Autret
12 would meet the claim because T(max) is earlier, which would show it's got
13 greater bioavailability than with the subcutaneous route.

14 MS. CORUZZI: Well, it's still an unreasonable interpretation of this
15 claim. When we first set out, we had a broader claim and we had dependent
16 claims for C(max), T(max) and AUC. The examiner restricted us out and
17 made us pick one, and we picked the one with the two parameters, C(max)
18 and bioavailability, which we've always interpreted as AUC. So even the
19 examiner given that restriction could not be looking at T(max), nor did he in
20 interpreting Autret. The examiner's position is that bioavailability can be
21 measured by
22 C(max) or the AUC, and that's the reason he's picking on Autret.

23 JUDGE HORNER: But he says in page 5 of the answer, Autret
24 discloses intradermal injection of a hormone resulting in a pharmacokinetic
25 profile similar to subcutaneous delivery but with a higher plasma level and

1 bioavailability, as assessed by C(max) and T(max), and he points to Figure
2 1. So I understand that to mean he's looking at T(max) as the measure of
3 bioavailability.

4 MS. CORUZZI: I'm sorry, where are you in the --

5 JUDGE HORNER: I'm on page 5 of the answer.

6 MS. CORUZZI: Page 5 of the answer.

7 JUDGE HORNER: The second full paragraph.

8 MS. CORUZZI: But Autret doesn't use T(max) as a parameter for
9 reaching the conclusion that bioavailability is the same or different in his
10 experiment. And if you go to Table 1 of Autret, again, he's equating AUC --
11 I mean, the table says AUC, ID, sub-Q and then biodisponibilité, which is
12 bioavailability. So Autret is not using T(max) at all in his discussion of
13 bioavailability and in his statement concerning no difference in
14 bioavailability between ID and sub-Q. And again, the Merck manual
15 discounts T(max) as a way to measure bioavailability, so that would be
16 consistent with the treatise that the skilled artisan would look at.

17 I mean, the examiner is trying, I mean, he's trying to use C(max) and
18 T(max). He's wrong, and that's evidenced by Merck, Autret itself, which
19 does not use either C(max) or T(max) when it discusses biodisponibilité or
20 bioavailability. And again, the examiner's 103 analysis hinges on this
21 incorrect interpretation of bioavailability. So you could drag in Autret and
22 say don't mind what Autret says, just look at these two numbers that Autret
23 himself did not use when Autret was describing bioavailability.

24 So, if you agree with me that the examiner has taken an unreasonable
25 interpretation of the claim, then you should reverse on the basis that Autret

1 just doesn't fit the bill. None of the references have a PK, that's the only one
2 with a PK, and its PK does not fit the requirement of the claim. And that's
3 also underscored by Dr. Kasting, who interpreted the claim as requiring an
4 increased AUC and came to the conclusion that Autret does not have what it
5 takes to anticipate the claim or make it obvious.

6 JUDGE HORNER: Okay. Well, we've run up against your 20
7 minutes, so if you want to wrap up.

8 MS. CORUZZI: Okay. I guess the other thing, if we can, the other
9 problem that the examiner has engaged in is hindsight reconstruction. And
10 it's all briefed, but I think one of the most egregious things is he's just taken
11 measurements from our application and grafted them into the prior art
12 without any explanation of how you get there. And I've tried to calculate
13 and figure out how did he get these numbers. He got the numbers from our
14 specification.

15 JUDGE HORNER: And you're talking about the length of the needle
16 now?

17 MS. CORUZZI: Right.

18 JUDGE HORNER: Okay.

19 MS. CORUZZI: The needle outlet. And in essence, I think here, if
20 you look at 103, which is the only issue here from the KSR point of view,
21 103 bars patentability unless the improvement is more than the predictable
22 use of prior art elements according to their established function. So, in our
23 case, there's no known relationship between the orifice and the requirement
24 of keeping the orifice in that narrow targeted area and the resulting PK when
25 the appropriate pressures are applied. So, in the absence of that known

1 relationship, it can't be said that this is routine experimentation of known
2 variables because it was an unknown variable. That's the invention. And a
3 case I'd like to cite that I think supports us on this is the recent Federal
4 Circuit decision In re: Cyclobenzaprine, 676 F.3d 1063, and that just came
5 down I think this month. Thank you. Sorry. April 2012. And another
6 recent Board decision, Ex parte McLaughlin, and this is Appeal No. 2009-
7 001294.

8 So here, hindsight reconstruction, incorrect claim construction, to
9 cobble together a facsimile of the invention that doesn't really exist in the
10 prior art.

11 JUDGE HORNER: Okay.

12 MS. CORUZZI: Okay.

13 JUDGE HORNER: Thank you.

14 MS. CORUZZI: Thank you.

15 (Whereupon, at 1:30 p.m., the proceedings were concluded.)